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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

JARRELL, NOBLE E

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/533,906	Applicant(s) MAECKE ET AL.	
	Examiner Noble Jarrell	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11 and 15-18 is/are pending in the application.
- 4a) Of the above claim(s) 4-9 and 15-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 11 is/are rejected.
- 7) ☒ Claim(s) 2 and 3 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 May 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/10/07</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION***Election/Restrictions***

1. Applicant's election with traverse of group I in the reply filed on 4/21/08 is acknowledged. The traversal is on the ground(s) that the Heppeler et al. reference does not constitute prior art for claim 4. This argument is found persuasive. It is not considered prior art for claim 4 because claim 4 does not allow for a compound with 3 CH₂-BOC groups. However, compound 5 in Heppeler et al. is considered prior art for claim 1 because 3 of the nitrogen atoms within the 1,4,7,10-tetraazadodecane ring are attached to CH₂-CO₂*t*-Bu groups, which are considered protected sidechains. The remaining amino group is attached to a octreotide (see compound 6 for octeotride). The reference is indeed good for what it shows.

The requirement is still deemed proper and is therefore made **FINAL**.

2. Claims 4-9 and 15-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/21/08.

Drawings

3. The drawings are objected to because there is no brief description of the figures in the specification. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The

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figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds where $n=4$ and the ring is 1,4,7,10-tetrazadodecane, does not reasonably provide enablement for compounds with other ring sizes as well as rings with 5 or 6 nitrogens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Applicants

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only show the preparation of 1,4,7,10-tetraazadodecane rings coupled to different octreotides (8-mer peptides).

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to tetraazadodecane rings coupled to bioactive effectors and a method of making the same.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Heppeler et al. (*Chemistry: A European Journal*, **1999**, 5(7), 1974-81, published online June 24, 1999) teach compounds that fall within the genus of claim 1 (see 102(a) rejection).

(5) The relative skill of those in the art:

One of ordinary skill in the art can replicate the procedure of producing compound 6d in the specification.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

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The specification has provided guidance only for the preparation of 1,4,7,10-tetraazadodecane rings coupled to different octreotides.

However, the specification does not provide enablement for other compounds that are encompassed under the scope of claim 1.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claim 1 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is indefinite for the following reasons: one, what ring size is being claimed? The connecting chain between each of the nitrogens can be a chain of any length. Two, what do applicants consider a "bioactive effector molecule"? This molecule can be a protein, a DNA molecule, or a fat, for example. Three, what protected sidechain is attached to each of the nitrogen atoms? Applicants only show a $\text{CH}_2\text{-CO}_2t\text{-Bu}$. What radiolabel is being associated with a polyazamacrocyclic of claim 1?

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8. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the exact steps to attach a radiolabelled compound to a compound of claim 1.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Heppeler et al. (*Chemistry: A European Journal*, **1999**, 5(7), 1974-81, published online June 24, 1999, cited in IDS). Heppeler et al. teach compound 5, an intermediate in the synthesis of preparation of compound 6. In compound 5, three of the nitrogen atoms in the 1,4,7,10-tetraazadodecane are substituted with CH₂-CO₂*t*-Bu (a protected sidechain) and the remaining nitrogen atom is substituted with D-Phe¹-Tyr²-octreotide. Attached to the molecule through a CH₂C(O) group.

Allowable Subject Matter

11. Claims 2 and 3 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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12. The following is a statement of reasons for the indication of allowable subject matter: Heppeler et al. teach compound 4 (scheme 1, page 1975). This compound fails to anticipate or render obvious compounds of claims 2 or 3 because a $\text{CH}_2\text{CO}_2t\text{-Bu}$ group is not considered an obvious variant of a $\text{CH}(\text{C}_{0-5}\text{CO}_2\text{H})\text{CO}_2t\text{-Bu}$ group.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

**/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624**